REMARKS

Upon entry of the above amendment, claims 13-29, 34, 36, and 42-56 will be pending in the application, new claims 52-56 having been added. Support for the new claims can be found throughout the application, including at page 5, lines 13-14. Claims 49-51 are amended to make them consistent with the other independent claims by adding text that was inadvertently omitted. Support for this amendment can be found in the claims as originally filed and in the specification, e.g., at page 2, lines 24-25. No new matter has been added.

All of the claims are presently under examination and have been rejected. The rejections are discussed below.

Rejection for Obviousness-type Double Patenting

The Office action mailed September 19, 2008 (the "Office action") provisionally rejects claims 13-15, 17, 19, 20, 22-25, 34, 36 and 42 for obviousness-type double-patenting over certain claims of copending U.S. Patent Application No. 09/367,950. Applicant intends to file a terminal disclaimer in one of the two applications if such is still deemed appropriate once the claims of one of the two applications are allowed.

Rejections under 35 USC § 103(a) for Obviousness

Claims 13-15, 17, 18, 20-29, 34, 36, and 42-51 were rejected as obvious over a single reference, Carling et al., WO 9311773 A1 ("Carling"). Applicant traverses the rejection.

The independent claims pending in the case are claims 13, 36, 42, and 49-51. All are included in the present rejection, as are several dependent claims. Claim 13 reads as follows:

> 13. A method of treating asthma in a patient, the method comprising administering an effective amount of a composition comprising, in admixture:
>
> (a) a first active ingredient that is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and
>
> (b) a second active ingredient that is budesonide;
>
> characterized in that the patient is administered (i) a maintenance dose of the composition twice per day, on a regular basis, and (ii) one or more additional doses on an irregular basis, wherein the one or more additional doses are administered as-needed, as determined by the patient.

Claims 36, 42 and 49 are similar to claim 13 except for the "wherein" clause at the end: "wherein the one or more additional doses are administered when the patient expects to encounter an asthma inducing condition" (claim 36); "wherein the one or more additional doses are administered when the patient experiences an acute asthma attack" (claim 42); and "wherein the one or more additional doses are administered when needed for symptom relief" (claim 49). Claims 50 and 51 (as amended) recite:

> 50. A method of treating asthma in a patient, the method comprising administering an effective amount of a composition comprising, in admixture:
>
> (a) a first active ingredient that is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and
>
> (b) a second active ingredient that is budesonide;
>
> characterized in that the patient is administered (i) a maintenance dose of the composition on a regular basis as determined by the patient's physician, and (ii) one or more additional doses on an irregular basis, wherein the one or more additional doses are administered when the patient determines the additional dose or doses are needed for symptom relief or when the patient expects to encounter an asthma inducing condition.

> 51. A method of treating asthma in a patient, the method comprising administering one or more doses of an effective amount of a composition comprising, in admixture:
>
> (a) a first active ingredient that is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and
>
> (b) a second active ingredient that is budesonide;
>
> characterized in that the patient is administered the one or more doses of the composition on an irregular basis when the patient determines the one or more doses are needed for symptom relief or when the patient expects to encounter an asthma inducing condition.

Claims 13, 36, 42 and 49 therefore require that the patient be administered the combination of formoterol and budesonide in both (i) a maintenance dose twice per day, on a regular basis, and (ii) one or more additional doses on an irregular basis. Claim 50 requires that the patient be administered the combination in both (i) a maintenance dose on a regular basis as determined by the patient's physician, and (ii) one or more additional doses on an irregular basis. Claim 51 requires that the patient be administered one or more doses of the composition on an irregular

basis when the patient determines they are needed for symptom relief or when the patient expects to encounter an asthma inducing condition.

Carling teaches a composition containing the combination of formoterol and budesonide. According to Carling at page 4, lines 19-21, "**The combination according to present invention permits a twice daily dosing regime as a basic treatment of asthma, particularly nocturnal asthma**." (Emphasis added.) Carling then emphasizes that this is the appropriate dosing regime by reiterating on page 6, lines 22-23, "**The intended dose regimen is a twice daily administration**." It is therefore undisputable what Carling intended to convey in his disclosure: that the combination of formoterol and budesonide should be administered on a regular basis, *twice per day, no more and no less*. That is "the intended dose regimen," according to Carling's explicit statement quoted above. Such a twice per day regimen is standard "maintenance therapy" for asthma, typically used where the drug being inhaled includes a slow-acting steroid drug such as budesonide that cannot relieve the immediate symptoms of an acute asthma attack, but is useful to reduce over the long term the chronic inflammation that, if uncontrolled, can contribute to the frequency of acute asthma attacks. Since steroids carry with them a high risk of dangerous side effects from overdosing, those of skill in the art prior to the present invention understood that the dosing and timing of steroid administration must be strictly controlled by the patient's doctor, and never left to the patient's discretion. See the extensive evidence supporting this understanding in the art supplied with applicant's Response filed July 27, 2007. Applicant has thoroughly established that applicant's interpretation of Carling as teaching twice per day, no more and no less is how one of ordinary skill in the art would have interpreted Carling.

In marked contrast to what was taught by Carling and was standard in the art, claim 13 requires that the patient be administered the combination in both (i) a maintenance dose twice per day, on a regular basis (similar to the maintenance therapy taught by Carling); and (ii) one or more additional doses on an irregular basis, wherein the one or more additional doses are administered as-needed, as determined by the patient (a concept the Office action at page 6 acknowledges is taught nowhere in Carling). Carling says nothing about the possibility of giving more doses beyond the recommended maintenance dose of twice per day, and certainly does not

contemplate that any additional doses be administered on an irregular basis, as determined by the patient. Permitting the dose of budesonide (or any steroid) to fluctuate from day to day at the patient's discretion was a radical idea when applicant first proposed it. Until applicant proved that administration in accordance with the invention was not only safe but also highly beneficial, it was accepted dogma that there was no point in administering budesonide (or any other steroid) at the time when an asthma attack was coming on. Because there was no expected advantage in administering budesonide when in the throes of an attack, and doing so would carry an unacceptable risk that the patient would end up taking a dangerously high amount of budesonide on some days, the art knew to strictly warn the patient not to administer a steroid-containing inhaler more than the twice per day recommended on the product label. This was all established by evidence provided in applicant's Response filed July 27, 2007. See that Response at pages 15-22, citing and describing Exhibits 1-5 that were submitted with that Response.

The Office action at page 6 says "**Carling et al. teaches suitable daily asthmatic dose of formoterol...and budesonide twice a day (i.e. on demand; see page 4, lines 24-28; page 6, lines 5-30...)"** (emphasis added). Thus, although explicitly acknowledging the fact that Carling teaches "twice a day" administration, the Office action then inexplicably seems to equate "twice a day" with "on demand," and cites some pages from Carling supposedly in support. Applicant does not see how anyone could possibly equate the term "twice a day" with "on demand", as "on demand" of course means whenever the patient decides to take it. The disclosure from Carling cited in the above quote from the Office action (i.e., page 4, lines 24-28; and page 6, lines 5-30 of Carling) does not say anything to support the Examiner's equating "twice a day" with "on demand." Page 4, lines 24-28, of Carling says only that formoterol and budesonide can be formulated "for simultaneous, sequential or separate administration by inhalation in the treatment of respiratory disorder." That says nothing about frequency or "on demand." Page 6, lines 5-30, of Carling lists various salts of formoterol, states that the range of formoterol to budesonide can be 1:4 to 1:70, and concludes:

> The intended dose regimen is a twice daily administration, where the suitable daily dose of formoterol is in the range of 6 to 100 μg with a preferred dose of 6-48 μg and the suitable daily dose for budesonide is 50 to 4800 μg with a preferred dose of 100-1600 μg.

> The particular dose used will strongly depend on the patient (age, weight etc) and the severity of the disease (mild, moderate, severe asthma etc). (Emphasis added)

Thus, the cited text from page 6 also does not support the Examiner's allegation that Carling teaches administration "on demand;" to the contrary, this text simply reiterates the "twice daily administration" instruction. Clarification as to what the Examiner intended by the sentence that attempts to link "twice a day" and "i.e. on demand" is requested so that applicant can respond.

On page 8 of the Office action, the Examiner acknowledges the obvious fact that Carling does not teach certain limitations of the independent claims:

> Carling et al. does not specifically teach one or more additional doses on an irregular, as-needed basis for rescue purposes, as determined by the patient (claim 13), based on the patient's symptoms, when (1) the patient experiences an increase in asthma symptoms as set forth in applicant's claim 13; or (2) when the patient is expecting to encounter an asthma inducing condition....(applicant's claims 34, 36, 50 and 51). Carling et al. does not teach to inhale additional doses as needed to improve control and provide acute relief (applicant's claim 42).[1] (Emphasis added)

Applicant agrees with the Examiner that Carling does not teach those limitations. However, the Office action then asserts that these would have been obvious modifications:

> To one of ordinary skill in the art, it would have been obvious to combine the method of Carling et al. and administering the method on an irregular, as-needed basis for rescue purposes, as determined by the patient in any of the circumstances detailed in claims 13, 34, 36, 42 and 49-51 because Carling et al. teaches that the dosages strongly depends on the severity of disease, whether mild, moderate, or sever asthma (see pg 6, lines 27-29), and the suitable daily dosage is up to 8 inhalation (see page 7-9).
>
> The motivation to combine the methods and compositions of Carling et al. and instructing the patient to inhale, on demand in any of the circumstances detailed in claims 13, 34, 36, 42 and 49-51 because Carling et al. teaches that the dosages strongly depends on the severity of disease and to achieve maximum benefit of daily dosage recommended. (Informal English and spellings in the original)

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[1] Applicant notes that this text quoted from the Office action is not an entirely accurate recitation of what the claims actually say. For example, claim 13 as currently presented says nothing about "rescue purposes" or "symptoms," and claim 42 says nothing about improving control or providing acute relief. Applicant urges the Examiner not to misrepresent the language of the claims, as that could contribute to misunderstandings of the scope of the claims post-issuance.

The Examiner's conclusion that this all would have been "obvious" is based, not on factual evidence about what one of ordinary skill in the art would have known at the time of the invention, but rather on what applicant submits are fundamentally invalid assumptions. The Examiner points to the teaching at page 6 of Carling that the particular dose used "will strongly depend on the patient (age, weight etc) and the severity of the disease (mild, moderate, severe asthma etc)," interpreting that to mean that the patient can decide for himself to take more than just two administrations per day (up to a maximum of eight administrations spread out over the day, totaling up to 100 μg formoterol)[2] if he is experiencing an acute asthmatic attack. See the Office action at page 9. Applicant submits that this is simply not a reasonable interpretation of what Carling teaches.

Rather than teach that the patient can decide whether and how many doses to take on any given day, Carling explicitly states that the intended dosing regimen is twice per day. The statements in that regard that appear at page 4, lines 19-21, and page 6, lines 22-23, of Carling were quoted above. In fact, the statement at page 6 about twice per day is the first part of the sentence on which the Office relies for the teaching "where the suitable daily dose of formoterol is in the range of 6 to 100 μg." To emphasize this point, the sentence is reproduced here:

> The intended dose regimen is a twice daily administration, where the suitable daily dose of formoterol is in the range of 6 to 100 μg with a preferred dose of 6-48 μg and the suitable daily dose for budesonide is 50 to 4800 μg with a preferred dose of 100-1600 μg.

That sentence, read in its entirety, makes it clear that Carling is saying the intended *twice daily* administrations can provide a daily total of formoterol in the range from 6 to 100 μg, i.e., the total daily dose of 6 to 100 μg formoterol should be split into two administrations per day. The total daily dose of 6 to 100 μg formoterol is inextricably linked to the twice daily administration regimen by the word "***where***", indicating Carling's intent to teach what range of dosage should be administered in the intended twice daily administration. The Office inexplicably ignores the directive in the first part of the sentence regarding "twice daily administration" in order to read

[2] The Examiner apparently derives the notion of "up to 8 inhalation" from Carling's teachings at page 6, lines 32-24, that "a suitable daily dose of formoterol is in the range of 6 to 100 μg," combined with the various examples on pages 7-9 of Carling illustrating that an inhaler can deliver a single dose of formoterol as low as 12 μg, i.e., approximately 1/8 of the proposed 100 μg maximum daily dose of formoterol.

into Carling a nonexistent instruction to the patient to take any desired number of doses up to a maximum total daily dose of 100 μg, and to administer the doses however many times each day the patient desires to do so. As applicant noted in the prior Response filed July 27, 2007, those of skill in the art understood that budesonide should be administered only as a maintenance treatment, and no more than twice per day, consistent with applicant's (and not the Examiner's) reading of Carling.

Carling's statement at page 6, lines 27-29, that the particular dose used "will strongly depend on the patient (age, weight etc) and the severity of the disease (mild, moderate, severe asthma etc)" does not in any way contradict Carling's teaching that the formoterol/budesonide combination should be administered in a set dosage just twice per day, though the Examiner appears to believe it does. These factors are listed by Carling because they are some of the factors that the physician considers when deciding what set daily dose to prescribe for a given patient. Obviously the patient would not be handed an inhaler and told to take any amount (up to 100 μg of formoterol and up to 4800 μg budesonide) he desires, based on his own perception of what a person of his weight, age, and disease condition should take. Contrary to the Examiner's perception, Carling does not say that it would be safe for all patients to take the maximum dose disclosed by Carling—obviously the maximum daily dose that is safe for a given patient will depend on factors such as the patient's age and weight, as Carling says. It is up to the physician to decide what is safe for a given patient, and how much the patient will need to control his symptoms, and instruct the patient regarding how much to take in his twice-daily administrations. A patient that frequently has severe bouts of acute asthma attacks may be prescribed a larger fixed twice-daily dose than that prescribed for a patient who reports only mild and infrequent episodes. There is no teaching in Carling that the patient should decide for himself when to increase or decrease the daily dosage, and certainly no teaching that extra doses should be administered whenever the patient feels an attack coming on.

The Examiner's confusion may stem from a belief that each "administration" must involve only a single activation or "dose" of an inhaler such as an inhaler exemplified in Carling (delivering, e.g., 12 μg formoterol and 100 μg budesonide in each activation—see Carling at

page 8, lines 11-15). In fact, when a physician needs to prescribe a total daily dose for a given patient that is relatively high (e.g., because of the patient's age, weight, and/or severity of disease), she can simply tell the patient to inhale two or three or four doses from an appropriate inhaler each morning (all in immediate succession as part of a single "administration") and the same number each evening. Regardless of the number of doses inhaled at each of the two daily administrations, the number of daily administrations does not change. Nor does the total dose inhaled at each of the two daily administrations vary from day to day. The physician tells the patient exactly how many times per day to administer the combination (two) and exactly the number of inhalations (i.e., activations of the inhaler) per administration, and the patient is expected to follow this instruction to the letter. For example, if a physician decides, based on the age, weight, and general severity of disease of a given patient, that the patient should inhale an amount of Carling's formoterol/budesonide combination sufficient to deliver a total of 96 μg of formoterol each day (i.e., near the high end of the range specified by Carling), the patient could be given an inhaler as described on page 8, lines 11-15, and then told to inhale, every day, four 12 μg doses at one administration (e.g., every morning) and four more 12 μg doses at the second administration (e.g., in the evening). The eight doses needed to deliver the prescribed amount of 96 μg per day from the Carling inhaler are thus administered just twice per day, in accordance with Carling's teachings. There is no need to read into Carling a teaching that up to eight doses can be spread throughout the day and administered whenever the patient feels the need, and in fact reading that into Carling would be contrary to what he explicitly teaches about twice daily administration being the intended regimen.

Applicant provided evidence in the Response filed July 27, 2007, about how Carling's teachings would have been understood in the art. Applicant also supplied with that July 27, 2007 Response extensive evidence of teaching-away in the art; surprising results; long-felt, unsatisfied need; and skepticism of experts, all of which the Examiner found to be "not persuasive" both in the October 18, 2007, Office action and again in the present Office action. The Examiner's comments on pages 12-14 of the present Office action are addressed below.

On page 12 of the present Office action, the Examiner reiterates her belief that Carling's statement, "the particular dose used will strongly depend on the patient (age, weight etc) and the severity of the disease (mild, moderate, severe asthma etc)," means that the patient should decide for him or herself how large a dose to take on any given day. Applicant has previously stated, and continues to stress, that this interpretation of Carling is simply unwarranted, particularly given what the art knew about the dangerous side effects of steroid drugs. Those of skill in the art knew that steroid use must be minimized and that only the prescribing physician can make such a judgment for her patients. The patient with no medical training would have no way to judge what would be safe. That is all clear from the evidence that applicant has already supplied. The Examiner appears to assume that, so long as the total daily dosage remains with the range of 6-100 μg formoterol and 50-4800 μg budesonide described in Carling at page 6, lines 24-26, the dosage will be safe for all patients. This assumption is simply unwarranted. Carling does not say that all doses within the stated ranges will be safe for all patients, and certainly does not say that the total daily dose for any given patient can vary from day to day within those ranges. He merely says that a suitable daily dose for any given patient will lie somewhere within those ranges, and will depend on the listed factors. It is up to the physician, not the patient, to select the appropriate daily dose, based on the factors.

Page 13 of the present Office action goes on to assert,

> Moreover, if the patient is experiencing acute asthmatic attack even with ongoing twice a day dosing regimen, the patient can still safely inhale an additional 6 inhalations without going over the maximum suitable daily dosage. In general, Carling et al. teaches therapeutic relief from asthmatic attack....Additionally, due to the urgency of therapy during an asthma attack, a patient would obviously seek relief with the medication without consulting with the physician, in knowing the safe daily dosage range of each medication.

Applicant emphatically disagrees. Carling certainly does not say that the maximum daily dosage specified in Carling will be suitable for all patients, and certainly does not say that the patient should use the combination when experiencing an acute asthmatic attack. The combination, according to Carling, is for twice-daily use, every day. Any use of this budesonide-containing combination other than for twice-daily maintenance therapy (e.g., for relief of an acute attack)

would have been contrary to Carling and contrary to what those of skill in the art knew to be appropriate use of budesonide, a highly potent steroid with (like any steroid drug) potentially dangerous side effects. Budesonide was never used in the art as a drug for providing immediate relief during an asthma attack. It is slow-acting, not immediate, and addresses only the underlying inflammation that contributes to the disease, not the bronchoconstriction that characterizes an acute asthma attack. Budesonide was understood in the art to be quite worthless for relieving an immediate attack, as it is not a bronchodilator. This is clear from the evidence supplied with the July 27, 2007 Response. Applicant cannot fathom why the Examiner believes, despite this evidence, that it would be "obvious" for a patient to seek relief from an urgent attack with a budesonide-containing composition.

Perhaps the problem stems from the Examiner's refusal to consider much of applicant's evidence, because she deems it "not commensurate [in] scope with the claimed invention." For example, the present Office action dismisses applicant's Exhibit 1 submitted with the July 27, 2007 Response because "Exhibit 1 is administration of budesonide as the sole active ingredient, while the claimed invention is an admixture of budesonide and formoterol." Applicant presented Exhibit 1, a 1997 product insert for Pulmicort® Turbuhaler®, in the July 27, 2007 Response as evidence that those of ordinary skill in the art understood that budesonide should always be administered in a regular, twice-daily regimen as maintenance therapy for asthma, and never used to relieve acute asthma attacks. See the detailed discussion of Exhibit 1 in the July 27, 2007 Response at pages 16-18. This teaching that taking extra doses of budesonide would be both pointless and dangerous strongly teaches away from use of any budesonide-containing product in the manner presently claimed. The Examiner appears to believe that, because Exhibit 1 concerns a product that contains only budesonide as an active ingredient, it cannot be used to support a teaching-away from the presently claimed methods. This is not a correct interpretation of the law regarding teaching-away. See, for example, the seminal case regarding teaching-away: *United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966) ("known disadvantage in old devices which would naturally discourage the search for new inventions may be taken into account in determining obviousness.") Applicant asks the Examiner to reconsider the evidence

of Exhibit 1 as a proper teaching-away from using a budesonide-containing product in accordance with the present invention. If she continues to dismiss this evidence simply because it does not concern budesonide formulated in the same combination product as used in the present claims, she is asked to provide legal support for her novel interpretation of the law. Exhibit 1 illustrates what was known at the time of the invention about using budesonide as a treatment for asthma. Given that knowledge in the art, it would not have been obvious to instruct patients to take Carling's budesonide-containing combination formulation more than twice per day, as needed, as determined by the patient—in fact, the art taught the opposite. In view of this teaching-away in the art, the rejection should be withdrawn.

Exhibit 2 attached to the July 27, 2007 Response is a product insert, circa 2001, for the formoterol/budesonide combination product as taught by Carling. As described in the July 27, 2007 Response at pages 18-19, Exhibit 2 shows that—even years after the present application's priority date—the art taught that Carling's combination product should be inhaled just twice per day, using a set dose prescribed by the physician, and while the dose could be varied by the physician, it was never to be varied by the patient even if the patient perceives the dose to be ineffective. See, for example, the statement in Exhibit 2: "If patients find the treatment ineffective, or exceed the current dose of the fixed combination, medical attention must be sought." The Examiner has not explained why that sentence from Exhibit 2 does not convince her that it was never left to the patient to decide to vary the dosage.

Exhibit 3 enclosed with the July 27, 2007 Response is the 2003 patient's instructions for use of Advair Diskus® fluticasone propionate/salmeterol xinafoate inhalation powder product. As explained in the July 27, 2007 Response at pages 19-20, this evidence was submitted to show that, consistent with the evidence regarding budesonide submitted as Exhibits 1 and 2, the art knew that steroid-containing compositions in general were to be inhaled only as a fixed maintenance therapy twice per day, and were NOT to be varied by the patient. The Examiner inexplicably dismisses this evidence solely because it concerns "two drugs not even claimed in the current application." Applicant asks the Examiner to reconsider this inappropriate dismissal of evidence submitted to show what those of skill in the art, even long after the present

application's priority date, considered to be proper use of steroid-containing drugs in treating asthma. It is certainly more probative on this point than is the Examiner's totally unsupported view of what she supposes would have been "obvious" based on Carling's disclosure.

On pages 13-14 of the Office action, the Examiner dismisses applicant's evidence of surprising results submitted as Exhibits 4 and 5 with the July 27, 2007 Response, commenting "the admixture is of budesonide, formoterol and terbutaline or budesonide and terbutaline, while the closest prior art is only the administration of the combination of budesonide and formoterol." (Emphasis in the original.) This suggests a misunderstanding of what is disclosed in these Exhibits. First, no "admixture of budesonide, formoterol and terbutaline" was used in the experiments disclosed in Exhibit 4 and discussed in Exhibit 5. The only "admixture" used in the trials disclosed in Exhibit 4 contained budesonide and formoterol. Second, the experimental arm of the trial employed the budesonide/formoterol composition exactly as recited in the present claims, for both maintenance treatment as well as when needed, at the discretion of the patient, as a "reliever" medication. Those patients did not use terbutaline as a reliever. One of the two control arms used the budesonide/formoterol combination just twice per day, as maintenance therapy only (as disclosed by Carling), while the other control arm used budesonide alone, twice per day for maintenance therapy. Both control arms relied on a separate inhaler containing terbutaline (a short-acting bronchodilator) where necessary for relief. Providing some sort of reliever medication is essential in any clinical trial involving an asthma medication, for if the maintenance therapy alone is insufficient to control the patient's symptoms and an acute episode ensues, the patient needs access to immediate relief. (In the experimental arm, the patients used the budesonide/formoterol combination for both maintenance therapy and reliever medication, so did not need terbutaline.) The Examiner appears to believe that, since Carling didn't mention use of terbutaline, use of terbutaline in the control arms somehow renders the results obtained in the Exhibit 4 clinical trials automatically invalid as evidence of surprising results. Applicant asks the Examiner to reconsider this extraordinary and illogical position. If anything, omitting use of terbutaline from the control arms in the Exhibit 4 trials would have resulted in worse results from the control arms, and consequently the results obtained with the experimental arm

would have appeared even better by comparison. The Examiner has not suggested any flaw in this logic, and has not addressed the unexpectedness of the Exhibit 4 results other than to reiterate her interpretation of Carling once more at page 14 of the present Office action. Merely repeating her interpretation of Carling does not explain why the Examiner believes one of ordinary skill in the art would have found the Exhibit 4 results unsurprising. And Exhibit 5 (the Barnes editorial) submitted with the July 27, 2007 Response showed that in fact one of skill in the art even several years after Carling was published found the Exhibit 4 results to have been "remarkable" and "surprisingly good results," and said it "may lead to changes in the paradigm of asthma management." This evidence of how one of skill in the art (Barnes) viewed the Exhibit 4 results even long after Carling had been published was pointed out in the July 27, 2007 Response at pages 27-28, but the Examiner has not addressed it. Nor has the Examiner supplied one shred of factual evidence to rebut the many examples of objective, factual evidence supplied by applicant. Applicant submits that all of the evidence of record strongly supports applicant's position that the presently claimed method was neither disclosed in nor obvious in view of Carling.

Claims 16 and 19 were rejected as obvious over Carling in view of Aberg et al. and in further view of Ryrfeldt et al. See the present Office action at pages 10-11. Claims 16 and 19 depend from claim 13, further limiting the formoterol to the R,R enantiomer of formoterol (claim 16) and the budesonide to the 22R epimer of budesonide (claim 19). Carling is cited as described above. Aberg et al. is cited for its teaching of the (R,R) isomer of formoterol, as required by claim 16. Ryrfeldt et al. is cited for its teaching of the 22R epimer of budesonide, as required by claim 19. As discussed in detail above, claim 13 is not obvious in view of Carling. Neither Aberg et al. nor Ryrfeldt et al. supplies what is missing from Carling with respect to claim 13. Accordingly, dependent claims 16 and 19, like the rest of the claims pending in the application, are not obvious over the cited art.

Withdrawal of the rejections for obviousness and allowance of the claims is respectfully requested.

The fees in the amount of $1,110.00 for a Petition for Three Month Extension of Time and $260.00 for excess claim fees are being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 06275-188002.

Respectfully submitted,

Date: March 18, 2009

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